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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,229	01/16/2007	Ozlem Tureci	VOS-203	4951

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EXAMINER	
GODDARD, LAURA B	
ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,229	TURECI ET AL.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-60 and 115-118* is/are pending in the application.

4a) Of the above claim(s) *57-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *115-118* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed on April 20, 2009 to the restriction requirement of January 22, 2009 has been received. Applicant has elected Group III, claims 57-60, drawn to the special technical feature of a method of diagnosing a disease characterized by expression or abnormal expression of a tumor-associated antigen, which method comprises administering an antibody binding to said tumor-associated antigen or to part thereof and coupled to a diagnostic agent for examination. Applicants further elected the species of sequence, SEQ ID NO:1.

Applicants canceled the elected claims and added new claims 115-118 drawn to the special technical feature of a method of diagnosing cancer in a patient or determining regression, course, or onset of cancer in a patient comprising detecting the level of a nucleic acid comprising SEQ ID NO:1 in a tissue sample. Claims 115-118 lack the same or corresponding special technical features from Groups I-V for the reasons set forth on pages 3-4 of the Restriction Requirement mailed January 22, 2009. Each SEQ ID NO is a species that does not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each SEQ ID NO is a structurally and functionally distinct molecule, hence they do not share the same or corresponding technical feature with each other.

Applicants have elected new claims 115-118 and the species of SEQ ID NO:1. Claims 57-60 and 115-118 are pending. Claims 57-60 are withdrawn from further consideration by the examiner under 35 CFR 1.142(b) as being drawn to a non-elected

invention. Claims 115-118 are currently being examined as drawn to the elected species of SEQ ID NO:1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 115-118 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for **a method for diagnosing melanoma in a patient, the method comprising detecting mRNA expression of SEQ ID NO:1 in a skin tissue sample from the patient**, does not reasonably provide enablement for a method for diagnosing any cancer in a patient or for determining regression, course or onset of any cancer, the method comprising detecting any level of a nucleic acid comprising SEQ ID NO:1 in any tissue sample from the patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed

invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method for diagnosing cancer in a patient, the method comprising detecting the level of a nucleic acid comprising SEQ ID NO:1 in a tissue sample from the patient and a method for determining regression, course, or onset of cancer in a patient, the method comprising detecting the level of a nucleic acid comprising SEQ ID NO:1 in a tissue sample from the patient.

The specification discloses identifying nucleic acid sequences of tumor associated antigens differentially expressed in tumors and discloses SEQ ID NO:1 (p. 4, lines 23-28; p. 5, line 5). The specification discloses that SEQ ID NO:1 mRNA was expressed in melanoma tissue samples but not detected in normal skin tissue samples (Figures 1 and 2; Example 3). The specification contemplates that the regression, course, or onset of a disease including cancer can be determined by monitoring a sample from a patient with cancer for abnormal expression of tumor associated antigens, or by determining

expression in the sample at a first and second time point to determine the course of disease (p. 16, lines 5-39).

One cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide guidance or examples for diagnosing **any cancer** comprising detecting **any level of SEQ ID NO:1** in **any tissue samples**. The specification discloses only a nexus between the detection of SEQ ID NO:1 mRNA in skin tissue samples and the diagnosis of melanoma. The specification fails to provide a nexus between the diagnosis of any cancer based on any levels of SEQ ID NO:1, including levels of zero, and diagnosis based on levels found in any tissue samples derived from any organs. Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker to successful clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test

the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Given the teaching of the art, without a validated nexus provided between SEQ ID NO:1 levels in any tissues and the presence of a specific cancer, one of skill in the art could not predictably use the claimed levels or tissues as a diagnostic agent to diagnose any cancers. A high quantity of experimentation would be required to determine which tissues provide what levels of SEQ ID NO:1 that would predictably diagnose which cancer.

Finally, one cannot extrapolate the disclosure of the specification to the scope of the claims because the specification does not provide guidance or examples for any methods of determining **regression, course, or onset** of any cancer. The specification does not provide a nexus between levels of SEQ ID NO:1 and a predictable determination of regression, course of cancer, or onset of cancer. The specification discloses only the detection of SEQ ID NO:1 mRNA in melanoma tissue sample and the absence of SEQ ID NO:1 mRNA in normal skin samples. Following the teaching of Tockman et al above, one of skill in the art could not reasonably extrapolate this data to the enablement of methods for determining regression, course, or onset of cancer

because the specification does not exemplify or identify any measurements of levels in SEQ ID NO:1 that predictably determine an regression, course, or onset of cancer. The single measurements of mRNA expression in each melanoma sample of Figures 1 and 2 do not indicate what stage cancer the patients have and do not determine cancer outcome, hence one of skill in the art could not determine if the cancer is regressing, what course the cancer is taking, and if it is the onset or beginning of cancer.

Therefore, in view of the state of the art, the quantity of experimentation necessary, the breadth of the claims, lack of guidance in the specification, and the absence of working examples for diagnosing any cancer and determining the regression, course, and onset of cancer based on any level of SEQ ID NO:1 in any tissue, it would require undue experimentation for one skilled in the art to practice the invention as broadly claimed.

3. **Conclusion:** No claim is allowed. The closest prior art appears to be GenBank Accession Number BU183861, a publicly available sequence on GenBank September 4, 2002 isolated from melanotic melanoma (see NCBI GenBank BU183861, p. 1-2, printed 6/19/2007, IDS). BU183861 is 100% identical to SEQ ID NO:1 of the instant application (see sequence search Result # 1, EST database, "20090528_121059_us-10-573-229a-1.rst"). Although BU183861 was isolated from melanotic melanoma, the sequence does not anticipate the claimed methods of cancer diagnosis and determining the regression, course, and onset of cancer because the sequence does not teach the claimed method steps. Further, methods of cancer diagnosis are not obvious over

BU183861 because BU183861 does not compare normal versus cancer (melanoma) expression of the BU183861 nucleic acid sequence, hence fails to provide a nexus between SEQ ID NO:1 mRNA expression in cancer (melanoma) versus expression in normal skin, and is not enabling for making a diagnosis of cancer.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642